

EXHIBIT 9

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Dated: October 10, 2008
Electronic Signature for Maria Laccotripe Zacharakis, Ph.D., J.D.: /MLZ./

Docket No.: BBI-093CPDV
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Jochen G. Salfeld *et al.*

Application No.: 10/884,830

Confirmation No.: 5175

Filed: July 1, 2004

Art Unit: 1646

For: HUMAN ANTIBODIES THAT BIND HUMAN
IL-12 AND METHODS FOR PRODUCING

Examiner: Bruce D. Hissong

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SUPPLEMENTAL AMENDMENT

Dear Sir:

This communication is supplemental to Applicants' Amendment and Response to Office Action filed December 4, 2007 and Supplemental Amendments filed February 27, 2008 and May 5, 2008.

Amendments to the Specification begin at page 2 of this communication.

Amendments to the Claims begin at page 3 of this communication.

Remarks begin at page 16 of this communication.

AMENDMENTS TO THE SPECIFICATION

Please amend the paragraph beginning at page 28, line 34, with the following replacement paragraph:

Figures 2A-2E show the CDR positions in the heavy chain of the Y61 antibody that were mutated by site-directed mutagenesis and the respective amino acid substitutions at each position. The graphs ~~at the right of the~~ presented in Figures 2A-1 through 2A-4, 2B-1 through 2B-4, 2C-1 through 2C-2, 2D-1 through 2D-4 and 2E-1 through 2E-2 figures show the off-rates for the substituted antibodies (black bars) as compared to unmutated Y61 (open bar).

Please amend the paragraph beginning at page 29, line 1, with the following replacement paragraph:

Figures 2F-2H show the CDR positions in the light chain of the Y61 antibody that were mutated by site-directed mutagenesis and the respective amino acid substitutions at each position. The graphs ~~at the right of the~~ presented in Figures 2F-1 through 2F-3, 2G-1 through 2G-2 and 2H-1 through 2H-3 figures show the off-rates for the substituted antibodies (black bars) as compared to unmutated Y61 (open bar).

Please amend the paragraph beginning at page 29, line 5, with the following replacement paragraph:

Figures 3A-3B demonstrates the *in vivo* efficacy of the human anti-IL-12 antibody J695, on plasma neopterin levels in cynomolgus monkeys.

AMENDMENTS TO THE CLAIMS

1-141. (Canceled).

142. (Currently amended) ~~An~~ A pharmaceutical composition comprising an isolated human antibody, or antigen-binding portion thereof, which is capable of binding to an epitope of the p40 subunit of IL-12 and an additional agent.

143. (Currently amended) The ~~antibody composition~~ of claim 142, wherein the antibody, or antigen-binding portion thereof, which is capable of binding to the epitope of the p40 subunit when the p40 subunit is bound to the p35 subunit of IL-12.

144. (Currently amended) The ~~antibody composition~~ of claim 142, wherein the antibody, or antigen-binding portion thereof, which is capable of binding to the epitope of the p40 subunit when the p40 subunit is bound to a p19 subunit.

145. (Currently amended) The ~~antibody composition~~ of claim 142, wherein the antibody, or antigen-binding portion thereof, which is capable of binding to the epitope of the p40 subunit when the p40 subunit is bound to the p35 subunit of IL-12 and when the p40 subunit is bound to a p19 subunit.

146. (Currently amended) ~~An~~ The isolated human antibody of claim 142, or antigen binding portion thereof, which is capable of binding wherein the antibody binds to an epitope of the p40 subunit of IL-12 to which an antibody selected from the group consisting of Y61 and J695 binds.

147. (Currently amended) The ~~antibody composition~~ of claim 142, wherein the antibody, or antigen-binding portion thereof, is further capable of binding to a first heterodimer and is also capable of binding to a second heterodimer, wherein the first heterodimer comprises the p40 subunit of IL-12 and the p35 subunit of IL-12, and wherein the second heterodimer comprises the p40 subunit of IL-12 and a p19 subunit.

148. **(Currently amended)** The ~~antibody~~ composition of claim 147, wherein the antibody, or antigen-binding portion thereof, neutralizes the biological activity of the first heterodimer.

149. **(Currently amended)** The ~~antibody~~ composition of claim 147, wherein the antibody, or antigen-binding portion thereof, neutralizes the biological activity of the second heterodimer.

150. **(Currently amended)** The ~~antibody~~ composition of claim 147, wherein the antibody, or antigen-binding portion thereof, neutralizes the biological activity of the first heterodimer and the second heterodimer.

151. **(Currently amended)** The ~~isolated antibody~~ composition of claim 148 or 150, wherein the antibody, or antigen binding portion thereof, ~~which~~ inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-9} M or less, or which inhibits human $IFN\gamma$ production with an IC_{50} of 1×10^{-10} M or less.

152. **(Currently amended)** The ~~isolated antibody~~ composition of any one of claims 142-145, wherein the antibody, or antigen binding portion thereof, ~~which~~ dissociates from the p40 subunit of IL-12 with a K_d of 1×10^{-10} M or less or a k_{off} rate constant of $1 \times 10^{-3} s^{-1}$ or less, as determined by surface plasmon resonance.

153-155. **(Canceled)**

156. **(Currently amended)** ~~An~~ The isolated human antibody of claim 142, or antigen binding portion thereof, which is capable of binding to an epitope of the p40 subunit of IL-12 and which has a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 25 and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 26;

157. **(Currently amended)** ~~An~~ The isolated human antibody of claim 142, or antigen binding portion thereof, which is capable of binding to an epitope of the p40 subunit of IL-12 and which has a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 27 and a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 28.

158. **(Currently amended)** ~~An~~ The isolated human antibody of claim 142, or antigen binding portion thereof, which is capable of binding to an epitope of the p40 subunit of IL-12 and which has a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 29 and a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 30.

159. **(Currently amended)** A pharmaceutical composition comprising an ~~An~~ isolated human antibody, or antigen-binding portion thereof, which is capable of binding to an interleukin comprising a p40 subunit and an additional agent.

160. **(Currently amended)** ~~The antibody composition~~ of claim 159, wherein the interleukin comprises a p40 subunit and a p35 subunit.

161. **(Currently amended)** ~~The antibody composition~~ of claim 160, wherein the interleukin is IL-12.

162. **(Currently amended)** ~~The antibody composition~~ of claim 159, wherein the interleukin comprises a p40 subunit and a p19 subunit.

163. **(Currently amended)** ~~The isolated antibody~~ antibody composition of any one of claims 159-162, wherein the antibody, or antigen binding portion thereof, ~~wherein the antibody~~ binds to an epitope of the p40 subunit.

164. **(Currently amended)** ~~An~~ The isolated human antibody of any one of claims 159-162, or antigen binding portion thereof, which is capable of binding to an interleukin comprising a p40 subunit, wherein the antibody binds to an epitope of the p40 subunit to which an antibody selected from the group consisting of Y61 and J695 binds.

165. **(Currently amended)** The ~~isolated antibody~~ composition of claim 159, wherein the antibody, or antigen binding portion thereof, ~~which~~ dissociates from the p40 subunit of the interleukin with a K_d of 1×10^{-10} M or less or a k_{off} rate constant of $1 \times 10^{-3} \text{ s}^{-1}$ or less, as determined by surface plasmon resonance.

166. **(Currently amended)** The ~~isolated antibody~~ composition of claim 159, wherein the antibody, or antigen binding portion thereof, ~~wherein the antibody~~ neutralizes the biological activity of the interleukin.

167. **(Currently amended)** The ~~isolated antibody~~ composition of claim 166, wherein the antibody, or antigen binding portion thereof, ~~which~~ inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-9} M or less, or which inhibits human $IFN\gamma$ production with an IC_{50} of 1×10^{-10} M or less.

168-170. **(Canceled)**

171. **(Currently amended)** ~~An The~~ isolated human antibody ~~of claim 159~~, or antigen binding portion thereof, which is capable of binding to an interleukin comprising a p40 subunit and which has a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 25 and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 26;

172. **(Currently amended)** ~~An The~~ isolated human antibody ~~of claim 159~~, or antigen binding portion thereof, which is capable of binding to an interleukin comprising a p40 subunit and which has a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 27 and a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 28.

173. **(Currently amended)** ~~An The~~ isolated human antibody ~~of claim 159~~, or antigen binding portion thereof, which is capable of binding to an interleukin comprising a p40 subunit and which has a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 29 and a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 30.

174. **(Currently amended)** A pharmaceutical composition comprising the antibody or an antigen binding portion thereof, of any one of claims ~~142-150~~ 146, 156-162 ~~156-158, 165-167~~ 164, and 171-173 and 223-225 and a pharmaceutically acceptable carrier.

175. **(Currently amended)** A composition comprising the antibody or an antigen binding portion thereof, of any one of claims ~~142-150~~ 146, 156-162 ~~156-158, 165-167~~ 164, and 171-173 and 223-225 and an additional agent.

176. **(Previously presented)** The composition of claim 175, wherein the additional agent is a therapeutic agent.

177. **(Previously presented)** The composition of claim 176, wherein the therapeutic agent is selected from the group consisting of budenoside, epidermal growth factor, corticosteroids, cyclosporin, sulfasalazine, aminosalicylates, 6-mercaptopurine, azathioprine, metronidazole, lipoxygenase inhibitors, mesalamine, olsalazine, balsalazide, antioxidants, thromboxane inhibitors, IL-1 receptor antagonists, anti-IL-1 β monoclonal antibodies, anti-IL-6 monoclonal antibodies, growth factors, elastase inhibitors, pyridinyl-imidazole compounds, antibodies or agonists of TNF, LT, IL-1, IL-2, IL-6, IL-7, IL-8, IL-15, IL-16, IL-18, EMAP-II, GM-CSF, FGF, and PDGF, antibodies of CD2, CD3, CD4, CD8, CD25, CD28, CD30, CD40, CD45, CD69, CD90 or their ligands, methotrexate, cyclosporin, FK506, rapamycin, mycophenolate mofetil, leflunomide, NSAIDs, ibuprofen, corticosteroids, prednisolone, phosphodiesterase inhibitors, adenosine agonists, antithrombotic agents, complement inhibitors, adrenergic agents, IRAK, NIK, IKK, p38, MAP kinase inhibitors, IL-1 β converting enzyme inhibitors, TNF α converting enzyme inhibitors, T-cell signalling inhibitors, metalloproteinase inhibitors, sulfasalazine, azathioprine, 6-mercaptopurines, angiotensin converting enzyme inhibitors, soluble cytokine receptors, soluble p55 TNF receptor, soluble p75 TNF receptor, sIL-1RI, sIL-1RII, sIL-6R, antiinflammatory cytokines, IL-4, IL-10, IL-11, IL-13 and TGF β .

178. **(Previously presented)** The composition of claim 176, wherein the therapeutic agent is selected from the group consisting of anti-TNF antibodies and antibody fragments

thereof, TNFR-Ig constructs, TACE inhibitors, PDE4 inhibitors, corticosteroids, budenoside, dexamethasone, sulfasalazine, 5-aminosalicylic acid, olsalazine, IL-1 β converting enzyme inhibitors, IL-1ra, tyrosine kinase inhibitors, 6-mercaptopurines and IL-11.

179. **(Previously presented)** The composition of claim 176, wherein the therapeutic agent is selected from the group consisting of corticosteroids, prednisolone, methylprednisolone, azathioprine, cyclophosphamide, cyclosporine, methotrexate, 4-aminopyridine, tizanidine, interferon- β 1a, interferon- β 1b, Copolymer 1, hyperbaric oxygen, intravenous immunoglobulin, clabribine, antibodies or agonists of TNF, LT, IL-1, IL-2, IL-6, IL-7, IL-8, IL-15, IL-16, IL-18, EMAP-II, GM-CSF, FGF, PDGF, antibodies to CD2, CD3, CD4, CD8, CD25, CD28, CD30, CD40, CD45, CD69, CD80, CD86, CD90 or their ligands, methotrexate, cyclosporine, FK506, rapamycin, mycophenolate mofetil, leflunomide, NSAIDs, ibuprofen, corticosteroids, prednisolone, phosphodiesterase inhibitors, adenosine agonists, antithrombotic agents, complement inhibitors, adrenergic agents, IRAK, NIK, IKK, p38 or MAP kinase inhibitors, IL-1 β converting enzyme inhibitors, TACE inhibitors, T-cell signalling inhibitors, kinase inhibitors, metalloproteinase inhibitors, sulfasalazine, azathioprine, 6-mercaptopurines, angiotensin converting enzyme inhibitors, soluble cytokine receptors, soluble p55 TNF receptor, soluble p75 TNF receptor, sIL-1RI, sIL-1RII, sIL-6R, sIL-13R, anti-P7s, p-selectin glycoprotein ligand (PSGL), antiinflammatory cytokines, IL-4, IL-10, IL-13 and TGF β .

180-198. **(Canceled)**

199. **(Canceled)** ~~A pharmaceutical composition comprising the antibody or an antigen binding portion thereof, of claim 151 and a pharmaceutically acceptable carrier.~~

200. **(Canceled)** ~~A composition comprising the antibody or an antigen binding portion thereof, of claim 151 and an additional agent.~~

201. **(Currently amended)** The composition of claim ~~200~~ 151, wherein the additional agent is a therapeutic agent.

202. **(Previously presented)** The composition of claim 201, wherein the therapeutic agent is selected from the group consisting of budenoside, epidermal growth factor, corticosteroids, cyclosporin, sulfasalazine, aminosalicylates, 6-mercaptopurine, azathioprine, metronidazole, lipoxigenase inhibitors, mesalamine, olsalazine, balsalazide, antioxidants, thromboxane inhibitors, IL-1 receptor antagonists, anti-IL-1 β monoclonal antibodies, anti-IL-6 monoclonal antibodies, growth factors, elastase inhibitors, pyridinyl-imidazole compounds, antibodies or agonists of TNF, LT, IL-1, IL-2, IL-6, IL-7, IL-8, IL-15, IL-16, IL-18, EMAP-II, GM-CSF, FGF, and PDGF, antibodies of CD2, CD3, CD4, CD8, CD25, CD28, CD30, CD40, CD45, CD69, CD90 or their ligands, methotrexate, cyclosporin, FK506, rapamycin, mycophenolate mofetil, leflunomide, NSAIDs, ibuprofen, corticosteroids, prednisolone, phosphodiesterase inhibitors, adenosine agonists, antithrombotic agents, complement inhibitors, adrenergic agents, IRAK, NIK, IKK, p38, MAP kinase inhibitors, IL-1 β converting enzyme inhibitors, TNF α converting enzyme inhibitors, T-cell signalling inhibitors, metalloproteinase inhibitors, sulfasalazine, azathioprine, 6-mercaptopurines, angiotensin converting enzyme inhibitors, soluble cytokine receptors, soluble p55 TNF receptor, soluble p75 TNF receptor, sIL-1RI, sIL-1RII, sIL-6R, antiinflammatory cytokines, IL-4, IL-10, IL-11, IL-13 and TGF β .

203. **(Previously presented)** The composition of claim 201, wherein the therapeutic agent is selected from the group consisting of anti-TNF antibodies and antibody fragments thereof, TNFR-Ig constructs, TACE inhibitors, PDE4 inhibitors, corticosteroids, budenoside, dexamethasone, sulfasalazine, 5-aminosalicylic acid, olsalazine, IL-1 β converting enzyme inhibitors, IL-1ra, tyrosine kinase inhibitors, 6-mercaptopurines and IL-11.

204. **(Previously presented)** The composition of claim 201, wherein the therapeutic agent is selected from the group consisting of corticosteroids, prednisolone, methylprednisolone, azathioprine, cyclophosphamide, cyclosporine, methotrexate, 4-aminopyridine, tizanidine, interferon- β 1a, interferon- β 1b, Copolymer 1, hyperbaric oxygen, intravenous immunoglobulin, clabribine, antibodies or agonists of TNF, LT, IL-1, IL-2, IL-6, IL-7, IL-8, IL-15, IL-16, IL-18, EMAP-II, GM-CSF, FGF, PDGF, antibodies to CD2, CD3, CD4, CD8, CD25, CD28, CD30, CD40, CD45, CD69, CD80, CD86, CD90 or their ligands, methotrexate, cyclosporine, FK506, rapamycin, mycophenolate mofetil, leflunomide, NSAIDs, ibuprofen, corticosteroids,

prednisolone, phosphodiesterase inhibitors, adenosine agonists, antithrombotic agents, complement inhibitors, adrenergic agents, IRAK, NIK, IKK, p38 or MAP kinase inhibitors, IL-1 β converting enzyme inhibitors, TACE inhibitors, T-cell signalling inhibitors, kinase inhibitors, metalloproteinase inhibitors, sulfasalazine, azathioprine, 6-mercaptopurines, angiotensin converting enzyme inhibitors, soluble cytokine receptors, soluble p55 TNF receptor, soluble p75 TNF receptor, sIL-1RI, sIL-1RII, sIL-6R, sIL-13R, anti-P7s, p-selectin glycoprotein ligand (PSGL), antiinflammatory cytokines, IL-4, IL-10, IL-13 and TGF β .

205. **(Canceled)** ~~A pharmaceutical composition comprising the antibody or an antigen binding portion thereof, of claim 152 and a pharmaceutically acceptable carrier.~~

206. **(Canceled)** ~~A composition comprising the antibody or an antigen binding portion thereof, of claim 152 and an additional agent.~~

207. **(Currently amended)** The composition of claim ~~206~~ 152, wherein the additional agent is a therapeutic agent.

208. **(Previously presented)** The composition of claim 207, wherein the therapeutic agent is selected from the group consisting of budenoside, epidermal growth factor, corticosteroids, cyclosporin, sulfasalazine, aminosalicylates, 6-mercaptopurine, azathioprine, metronidazole, lipoxygenase inhibitors, mesalamine, olsalazine, balsalazide, antioxidants, thromboxane inhibitors, IL-1 receptor antagonists, anti-IL-1 β monoclonal antibodies, anti-IL-6 monoclonal antibodies, growth factors, elastase inhibitors, pyridinyl-imidazole compounds, antibodies or agonists of TNF, LT, IL-1, IL-2, IL-6, IL-7, IL-8, IL-15, IL-16, IL-18, EMAP-II, GM-CSF, FGF, and PDGF, antibodies of CD2, CD3, CD4, CD8, CD25, CD28, CD30, CD40, CD45, CD69, CD90 or their ligands, methotrexate, cyclosporin, FK506, rapamycin, mycophenolate mofetil, leflunomide, NSAIDs, ibuprofen, corticosteroids, prednisolone, phosphodiesterase inhibitors, adenosine agonists, antithrombotic agents, complement inhibitors, adrenergic agents, IRAK, NIK, IKK, p38, MAP kinase inhibitors, IL-1 β converting enzyme inhibitors, TNF α converting enzyme inhibitors, T-cell signalling inhibitors, metalloproteinase inhibitors, sulfasalazine, azathioprine, 6-mercaptopurines, angiotensin converting enzyme

inhibitors, soluble cytokine receptors, soluble p55 TNF receptor, soluble p75 TNF receptor, sIL-1RI, sIL-1RII, sIL-6R, antiinflammatory cytokines, IL-4, IL-10, IL-11, IL-13 and TGF β .

209. **(Previously presented)** The composition of claim 207, wherein the therapeutic agent is selected from the group consisting of anti-TNF antibodies and antibody fragments thereof, TNFR-Ig constructs, TACE inhibitors, PDE4 inhibitors, corticosteroids, budenoside, dexamethasone, sulfasalazine, 5-aminosalicylic acid, olsalazine, IL-1 β converting enzyme inhibitors, IL-1ra, tyrosine kinase inhibitors, 6-mercaptopurines and IL-11.

210. **(Previously presented)** The composition of claim 207, wherein the therapeutic agent is selected from the group consisting of corticosteroids, prednisolone, methylprednisolone, azathioprine, cyclophosphamide, cyclosporine, methotrexate, 4-aminopyridine, tizanidine, interferon- β 1a, interferon- β 1b, Copolymer 1, hyperbaric oxygen, intravenous immunoglobulin, clabribine, antibodies or agonists of TNF, LT, IL-1, IL-2, IL-6, IL-7, IL-8, IL-15, IL-16, IL-18, EMAP-II, GM-CSF, FGF, PDGF, antibodies to CD2, CD3, CD4, CD8, CD25, CD28, CD30, CD40, CD45, CD69, CD80, CD86, CD90 or their ligands, methotrexate, cyclosporine, FK506, rapamycin, mycophenolate mofetil, leflunomide, NSAIDs, ibuprofen, corticosteroids, prednisolone, phosphodiesterase inhibitors, adenosine agonists, antithrombotic agents, complement inhibitors, adrenergic agents, IRAK, NIK, IKK, p38 or MAP kinase inhibitors, IL-1 β converting enzyme inhibitors, TACE inhibitors, T-cell signalling inhibitors, kinase inhibitors, metalloproteinase inhibitors, sulfasalazine, azathioprine, 6-mercaptopurines, angiotensin converting enzyme inhibitors, soluble cytokine receptors, soluble p55 TNF receptor, soluble p75 TNF receptor, sIL-1RI, sIL-1RII, sIL-6R, sIL-13R, anti-P7s, p-selectin glycoprotein ligand (PSGL), antiinflammatory cytokines, IL-4, IL-10, IL-13 and TGF β .

211. **(Canceled)** ~~A pharmaceutical composition comprising the antibody or an antigen binding portion thereof, of claim 163 and a pharmaceutically acceptable carrier.~~

212. **(Canceled)** ~~A composition comprising the antibody or an antigen binding portion thereof, of claim 163 and an additional agent.~~

213. **(Currently amended)** The composition of claim ~~242~~ 163, wherein the additional agent is a therapeutic agent.

214. **(Previously presented)** The composition of claim 213, wherein the therapeutic agent is selected from the group consisting of budenoside, epidermal growth factor, corticosteroids, cyclosporin, sulfasalazine, aminosalicylates, 6-mercaptopurine, azathioprine, metronidazole, lipoxygenase inhibitors, mesalamine, olsalazine, balsalazide, antioxidants, thromboxane inhibitors, IL-1 receptor antagonists, anti-IL-1 β monoclonal antibodies, anti-IL-6 monoclonal antibodies, growth factors, elastase inhibitors, pyridinyl-imidazole compounds, antibodies or agonists of TNF, LT, IL-1, IL-2, IL-6, IL-7, IL-8, IL-15, IL-16, IL-18, EMAP-II, GM-CSF, FGF, and PDGF, antibodies of CD2, CD3, CD4, CD8, CD25, CD28, CD30, CD40, CD45, CD69, CD90 or their ligands, methotrexate, cyclosporin, FK506, rapamycin, mycophenolate mofetil, leflunomide, NSAIDs, ibuprofen, corticosteroids, prednisolone, phosphodiesterase inhibitors, adenosine agonists, antithrombotic agents, complement inhibitors, adrenergic agents, IRAK, NIK, IKK, p38, MAP kinase inhibitors, IL-1 β converting enzyme inhibitors, TNF α converting enzyme inhibitors, T-cell signalling inhibitors, metalloproteinase inhibitors, sulfasalazine, azathioprine, 6-mercaptopurines, angiotensin converting enzyme inhibitors, soluble cytokine receptors, soluble p55 TNF receptor, soluble p75 TNF receptor, sIL-1RI, sIL-1RII, sIL-6R, antiinflammatory cytokines, IL-4, IL-10, IL-11, IL-13 and TGF β .

215. **(Previously presented)** The composition of claim 213, wherein the therapeutic agent is selected from the group consisting of anti-TNF antibodies and antibody fragments thereof, TNFR-Ig constructs, TACE inhibitors, PDE4 inhibitors, corticosteroids, budenoside, dexamethasone, sulfasalazine, 5-aminosalicylic acid, olsalazine, IL-1 β converting enzyme inhibitors, IL-1ra, tyrosine kinase inhibitors, 6-mercaptopurines and IL-11.

216. **(Previously presented)** The composition of claim 213, wherein the therapeutic agent is selected from the group consisting of corticosteroids, prednisolone, methylprednisolone, azathioprine, cyclophosphamide, cyclosporine, methotrexate, 4-aminopyridine, tizanidine, interferon- β 1a, interferon- β 1b, Copolymer 1, hyperbaric oxygen, intravenous immunoglobulin, clabribine, antibodies or agonists of TNF, LT, IL-1, IL-2, IL-6, IL-7, IL-8, IL-15, IL-16, IL-18,

EMAP-II, GM-CSF, FGF, PDGF, antibodies to CD2, CD3, CD4, CD8, CD25, CD28, CD30, CD40, CD45, CD69, CD80, CD86, CD90 or their ligands, methotrexate, cyclosporine, FK506, rapamycin, mycophenolate mofetil, leflunomide, NSAIDs, ibuprofen, corticosteroids, prednisolone, phosphodiesterase inhibitors, adenosine agonists, antithrombotic agents, complement inhibitors, adrenergic agents, IRAK, NIK, IKK, p38 or MAP kinase inhibitors, IL-1 β converting enzyme inhibitors, TACE inhibitors, T-cell signalling inhibitors, kinase inhibitors, metalloproteinase inhibitors, sulfasalazine, azathioprine, 6-mercaptopurines, angiotensin converting enzyme inhibitors, soluble cytokine receptors, soluble p55 TNF receptor, soluble p75 TNF receptor, sIL-1RI, sIL-1RII, sIL-6R, sIL-13R, anti-P7s, p-selectin glycoprotein ligand (PSGL), antiinflammatory cytokines, IL-4, IL-10, IL-13 and TGF β .

217. **(Canceled)** ~~A pharmaceutical composition comprising the antibody or an antigen binding portion thereof, of claim 164 and a pharmaceutically acceptable carrier.~~

218. **(Canceled)** ~~A composition comprising the antibody or an antigen binding portion thereof, of claim 164 and an additional agent.~~

219. **(Currently amended)** The composition of any one of claims 218 142-145, 147-150, 159-162 and 165-167, wherein the additional agent is a therapeutic agent.

220. **(Previously presented)** The composition of claim 219, wherein the therapeutic agent is selected from the group consisting of budenoside, epidermal growth factor, corticosteroids, cyclosporin, sulfasalazine, aminosalicylates, 6-mercaptopurine, azathioprine, metronidazole, lipoxigenase inhibitors, mesalamine, olsalazine, balsalazide, antioxidants, thromboxane inhibitors, IL-1 receptor antagonists, anti-IL-1 β monoclonal antibodies, anti-IL-6 monoclonal antibodies, growth factors, elastase inhibitors, pyridinyl-imidazole compounds, antibodies or agonists of TNF, LT, IL-1, IL-2, IL-6, IL-7, IL-8, IL-15, IL-16, IL-18, EMAP-II, GM-CSF, FGF, and PDGF, antibodies of CD2, CD3, CD4, CD8, CD25, CD28, CD30, CD40, CD45, CD69, CD90 or their ligands, methotrexate, cyclosporin, FK506, rapamycin, mycophenolate mofetil, leflunomide, NSAIDs, ibuprofen, corticosteroids, prednisolone, phosphodiesterase inhibitors, adenosine agonists, antithrombotic agents, complement inhibitors,

adrenergic agents, IRAK, NIK, IKK, p38, MAP kinase inhibitors, IL-1 β converting enzyme inhibitors, TNF α converting enzyme inhibitors, T-cell signalling inhibitors, metalloproteinase inhibitors, sulfasalazine, azathioprine, 6-mercaptopurines, angiotensin converting enzyme inhibitors, soluble cytokine receptors, soluble p55 TNF receptor, soluble p75 TNF receptor, sIL-1RI, sIL-1RII, sIL-6R, antiinflammatory cytokines, IL-4, IL-10, IL-11, IL-13 and TGF β .

221. **(Previously presented)** The composition of claim 219, wherein the therapeutic agent is selected from the group consisting of anti-TNF antibodies and antibody fragments thereof, TNFR-Ig constructs, TACE inhibitors, PDE4 inhibitors, corticosteroids, budenoside, dexamethasone, sulfasalazine, 5-aminosalicylic acid, olsalazine, IL-1 β converting enzyme inhibitors, IL-1ra, tyrosine kinase inhibitors, 6-mercaptopurines and IL-11.

222. **(Previously presented)** The composition of claim 219, wherein the therapeutic agent is selected from the group consisting of corticosteroids, prednisolone, methylprednisolone, azathioprine, cyclophosphamide, cyclosporine, methotrexate, 4-aminopyridine, tizanidine, interferon- β 1a, interferon- β 1b, Copolymer 1, hyperbaric oxygen, intravenous immunoglobulin, clabribine, antibodies or agonists of TNF, LT, IL-1, IL-2, IL-6, IL-7, IL-8, IL-15, IL-16, IL-18, EMAP-II, GM-CSF, FGF, PDGF, antibodies to CD2, CD3, CD4, CD8, CD25, CD28, CD30, CD40, CD45, CD69, CD80, CD86, CD90 or their ligands, methotrexate, cyclosporine, FK506, rapamycin, mycophenolate mofetil, leflunomide, NSAIDs, ibuprofen, corticosteroids, prednisolone, phosphodiesterase inhibitors, adenosine agonists, antithrombotic agents, complement inhibitors, adrenergic agents, IRAK, NIK, IKK, p38 or MAP kinase inhibitors, IL-1 β converting enzyme inhibitors, TACE inhibitors, T-cell signalling inhibitors, kinase inhibitors, metalloproteinase inhibitors, sulfasalazine, azathioprine, 6-mercaptopurines, angiotensin converting enzyme inhibitors, soluble cytokine receptors, soluble p55 TNF receptor, soluble p75 TNF receptor, sIL-1RI, sIL-1RII, sIL-6R, sIL-13R, anti-P7s, p-selectin glycoprotein ligand (PSGL), antiinflammatory cytokines, IL-4, IL-10, IL-13 and TGF β .

223. **(New)** The antibody of claim 164, wherein the interleukin comprises a p40 subunit and a p35 subunit.

224. **(New)** The antibody of claim 164, wherein the interleukin is IL-12.

225. **(New)** The antibody of claim 164, wherein the interleukin comprises a p40 subunit and a p19 subunit.

REMARKS

Applicants and their attorney thank the Examiner for the courtesy of the telephonic interviews of September 23 and 30, 2008. During the foregoing interviews, the Examiner indicated that claims 146, 156-158, 164, 171-173, 174¹, 175-179, 200-204, 206-210, 212-216, 217-222 do not interfere with the claims of U.S. Application No. 10/912,994 (hereinafter “the ‘994 application”). Without acquiescing to the validity of the Examiner’s determination and in the interest of expediting allowance of the present application, Applicants have cancelled herein the subject matter² of the allegedly interfering claims. Accordingly, Applicants respectfully request that the present application proceed to issuance.

Claims 142-152, 156-167, 171-179 and 199-222 were pending in the application. Claims 199, 200, 205, 206, 211, 212, 217 and 218 have been canceled without prejudice. Claims 142-152, 156-167, 171-175, 201, 207, 213 and 219 have been amended to incorporate the limitations of the dependent claims which the Examiner has indicated do not interfere with the claims of the ‘994 application. New claims 223-225 have been added. Accordingly, upon entry of the amendments presented herein, claims 142-152, 156-167, 171-179, 201-204, 207-210, 213-216 and 219-225 will remain pending in the application.

No new matter has been added. Support for the amendments to the claims can be found in the claims and throughout the specification as originally filed. Amendments to and cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner’s rejections and were done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

¹ As it depends from claims 146, 156-158, 164 and 171-173.

² As discussed with the Examiner, the independent claims have been amended to include the subject matter of the dependent claims that have been indicated by the Examiner as not interfering with the claims in the ‘994 application.

Supplemental Information Disclosure Statement

A supplemental Information Disclosure Statement is being submitted concurrently herewith in which Applicants make of record Paper No. 20 and Paper No. 128 of Patent Interference No. 105,592 involving parent patent US 6,914,128. As discussed with the Examiner in the telephonic interview of October 8, 2008 and as indicated in Paper No. 20, the Junior Party in the Interference, Centocor, had requested authorization to file a motion to designate claims 65-74 of parent patent US 6,914,128 as corresponding to Count 1 of the interference. As further indicated in Paper No. 20, Centocor's request was deferred to the priority phase of the interference, at which time Centocor was authorized to renew its request. As also discussed with the Examiner and as indicated in Paper No. 128, the priority phase began on August 22, 2008.

Claims Allegedly Interfering with the Claims in the '994 Application

Applicants respectfully submit that the subject matter of the claims deemed by the Examiner to allegedly interfere with the claims of the '994 application (*i.e.*, previously pending claims 142-145, 147-152, 159-163, 165-167, 174³, 199, 205 and 211) will be pursued by Applicants in a continuation application that will be filed shortly.

For example, claim 142 has been amended to incorporate the subject matter of claim 175. Similarly, claim 159 has been amended to incorporate the subject matter of claim 175.

³ As it depends from claims 142-145, 147-150, 159-162 and 165-167.

CONCLUSION

Reconsideration and allowance of all the pending claims is respectfully requested. If a telephone conversation with Applicants' Attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to Deposit Account No. 12-0080, under Order No. BBI-093CPDV.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Dated: October 10, 2008

Respectfully submitted,

By: Electronic signature: /MLZ/
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